

Fw: Consider model model simplification

Bob Benson to: Bill Brattin, David Berry

01/14/2011 02:58 PM

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This seems like a good suggestion to me.

----- Forwarded by Bob Benson/R8/USEPA/US on 01/14/2011 02:57 PM -----

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Subject: Consider model model simplification

Bob,

I would like to suggest one variant on your modeling that you may want to check out. That would be to fix $b_1=1$ in the model. In toxicology parlance, the simplified model would imply that you would be fitting a discrete Michaelis-Menten model - with your modification to have vary the intercept with latency - rather than a modification of a Hill model. The Michaelis-Menten based model will have some linear slope at low dose (may be steep, but would not become "infinitely steep" as get close to zero dose). Of course you would have find out through trying whether the simpler model provided an adequate fit to the data.

The reason I suggest trying this is that my hunch is Bill's bootstrap analysis is giving very low BMDL is because some of the bootstrap resamples have fits with Hill exponent (b_1 , that is) with values less than one. In that case, the Hill model can become extremely steep at the lowest doses (and infinitely steep as approach zero). Thus if the simpler Michaelis-Menten model works for the data set, it would seem that it may more likely yield plausible BMDL values.

Just offering this for your consideration...

Paul